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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,325	08/31/2001	Everett C. Pesci	UIZ-068CP	1369

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EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 04/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/945,325

Applicant(s)

PESCI ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 January 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-42 and 46-48 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-42 and 46-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3-42, 46-48 are pending. Claims 2, 43-45, 49-64 have been canceled according to the amendment filed on 1-9-2003,

Claim Rejections - 35 USC § 112

2. The rejection for Claims 1, 14-16, 19-40, 46-48 under 35 U.S.C. 112, second paragraph is withdrawn in view of the amendment.

Duplicate Claims

3. Applicant is advised that should claim 1 or 19 be found allowable, claims 20-34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 20-28 does not further limit the compound of claim 1 or 19. Should claim 1 be found allowable, claims 29-34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 29-34 does not further limit the compound of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the response, Applicant states that this issue will be address upon the allowance of claim 1 and 19.

4. The warning that Claim 33 being a duplicate of claim 34 is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

5. The rejection for Claims 1, 2, 4, 10-14, 19-28, 32-42, 46-48 under 35 U.S.C. 102(a) as being anticipated by Pesci (PNAS, 1999, 96(20):11229) is withdrawn in view of the 132

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Declaration by Dr. Pesci declaring that the Pesci paper discloses his own research and that of the named co-inventors since Susan McKnight is not a co-inventor of the subject matter disclosed.

6. The rejection for Claims 1, 14, 15, 20-40 under 35 U.S.C. 102(b) as being anticipated by Dekker (5942619 or WO 97/12868) is withdrawn in view of the amendment incorporating the limitation of Q as defined in claim 2 and that R5 is not H, thereby setting a demarcation from Dekker's compound wherein R5 is H.

7. The rejection for Claims 1-4, 9, 12, 14, 20-40 under 35 U.S.C. 102(b) as being anticipated by Guilhon (Phytochemistry, 1994, 37(4), 1193-1195) is withdrawn in view of the amendment incorporating the limitation of Q as defined in claim 2 and that R5 is not H, thereby setting a demarcation from Guilhon's compound wherein R5 is H.

8. The rejection for Claims 1, 14, 15, 20-40 under 35 U.S.C. 102(b) as being anticipated by Lee (J. Liq. Chrom. & Rel. Technol., 1997, 20(1), 63-78) is withdrawn in view of the amendment incorporating the limitation of Q as defined in claim 2 and that R5 is not H, thereby setting a demarcation from Lee's compound wherein R5 is H.

9. The rejection for Claims 1-4, 12, 14, 20-34 under 35 U.S.C. 102(b) as being anticipated by Beifuss (Synlett, 1997, 3, 313-315) is withdrawn in view of the amendment incorporating the limitation of Q as defined in claim 2 and that R5 is not H, thereby setting a demarcation from Beifuss's compound wherein R5 is H.

10. The rejection for Claims 1-4, 12, 14, 20-40, 46 under 35 U.S.C. 102(b) as being anticipated by Dibitus (J. Marine Biotechnology, 1998, 6, 136-141) is withdrawn in view of the amendment incorporating the limitation of Q as defined in claim 2 and that R5 is not H, thereby setting a demarcation from Dibitus's compound wherein R5 is H.

Claim Rejections - 35 USC § 112

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11. The scope rejection under 35 U.S.C. 112, first paragraph for claims 1, 3-42, 46-48 is maintained for reasons of record. The specification is only enabling for making and using 2-heptyl-3-hydroxy-4-quinolinone.

Applicant maintains that it is not necessary to provide written description for what is known by the skilled artisan, the specification therefore has provided enabling disclosure to make and use the invention as claimed.

While the number of working examples is not controlling, the scope of the claims must be commensurate with that of the objective enablement. In the instant case, the instantly claimed compound, other than 2-heptyl-3-hydroxy-4-quinolone, has not been described. A general procedure for making these unobvious compound has not been provided in the specification. Starting materials and procedures for making the instant compound other than 2-heptyl-3-hydroxy-4-quinolone (especially those compounds wherein R10-R24 are other than hydrogen, and wherein R2-4 are all halogen) are not seen in the specification but are required. Sources are particularly pertinent because absent sources, the public is offered mere language, rather than enablement. *Ex parte Moersch* 104 USPQ 122. *In re Howarthe* 210 USPQ 689.

Applicant argues that the unpredictability in Bycroft's homoserine lactone compounds is not applicable to the instant quinolone compound and is therefore conjecture. Further, applicant has amended claim 1 to exclude the quinolone compound shown not to activate *las B'-lacZ* (cited on page 24 of the specification, therefore the claims as amended are fully enabled.

However, the high degree of unpredictability is well-recognized in the autoinducer art. It is well known that a small change in the structure of the compound would drastically change its biological activity. Bycroft's homoserine lactone compounds are cited to illustrate this point because at the time of the invention, quinolone compounds as autoinducers have not been described. Indeed, 2-heptyl-3-hydroxy-4-quinolone as a cell-to-cell signaling molecule (PQS) has only been identified a few years ago. The art is therefore at an infancy stage. Moreover, since the specification expressly discloses that structurally similar analogs of 2-heptyl-3-hydroxy-4-quinolone do not activate *las B'-lacZ*, there is no basis to extrapolate the results of 2-heptyl-3-hydroxy-4-quinolone to compounds embraced by the claims which are structurally further removed from the inactive analog compounds. Although applicant has excluded these two inactive quinolone compounds from the claims, the fact remains that even within the structurally

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similar quinolone compounds, there exists a high degree of unpredictability, as recited on page 24, lines 34-38 of the specification.

Applicant argues that the term 'modulator' has been defined in the specification and can be determined without undue experimentation, and a working example is not required within the meaning of 112 first paragraph.

While it is clear that 'modulation' includes both enhancement and down regulation, it is unclear which of the inventive compound enhances and which inhibits, or both in the absence of any specific teachings in the specification. Although a working example is not required for enablement as applicant contends, some experimentation is permitted and every claimed embodiment need not be shown to possess the asserted activity, there should be a showing commensurate in scope with the claims. As stated in *In re Cavallito* 127, USPQ 202, "where the applicant seeks to obtain a monopoly in exchange for his disclosure of a group of compounds, there should be a disclosure which gives reasonable assurance that all, or substantially all of them are useful....an applicant is not entitled to a claim for a group of compounds merely on the basis of a showing that a selected few are useful and a general suggestion of a similar utility in the others". In the instant case, an example for a compound that 'modulates' the activity of PQS, either enhances or inhibits the autoinducer activity of PQS, 'modulates' or antagonize the activity of Las R and/or the RhIR proteins as recited in the instant claims 29-34 has not been described in the specification. Since the only compound shown is 2-heptyl-3-hydroxy-4-quinolinone (PQS), and no specific compounds that inhibit or enhance PQS are described, undue experimentation would be required for one of ordinary skill in the art to use these compounds as claimed. Furthermore, in the instant autoinducer art, where there is a high degree of unpredictability exists, the required disclosure will be greater than for the disclosure of an invention involving a predictable factor such as a mechanical or electrical element. In *re Vaeck*, 20 USPQ 2d 1438, especially when PQS is in its infancy stage.

In conclusion, in view of the state of the art, the high degree of unpredictability of the art, the absence of specific working examples, the scope of the claims does not commensurate with that of the objective enablement. Insufficient teaching and guidance have not been provided in the specification to enable one of ordinary skill in the art to practice the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 10-14, 19-28, 32-42, 46-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeda (Hakko Kogaku Zasshi (1959), 37, 59-63, abstract). The prior art compound, 2-heptyl-3-hydroxy-4-quinolone is also isolated from the culture of pseudomonas aeruginosa as in the instant, and it has been shown to have antibacterial activity. Although Takeda is silent on the various biological activities recited in the instant claims, these properties would be inherent in the prior art compound as it is identical to the instant compound.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 9, Y is O, or S has no antecedent basis in the base claim 1 wherein Y is NR9.

b. Claim 10, R5 is H has no antecedent basis in the base claim 1 since H has been deleted from the definition of R5.

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Specification/ Drawings

14. The specification is objected to because the figures in the specification do not come within the purview of 37 CFR 1.58(a), which permits only tables, chemical and mathematical formulas in the specification in lieu of formal drawings.

Formal drawings in accordance to 37 C.F.R. 1.81, 1.83-1.85 are required. See MPEP 608.01 and 608.02.

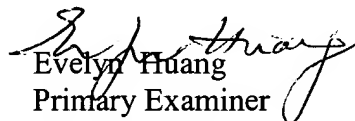
A brief description of the drawings is not found in the specification but is required.

In the response, Applicant states that this issue will be address upon the allowance of the claims.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
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March 12, 2003